REMARKS

Claims 21-36 are currently pending in the application. In an Office Action dated October 3, 2002 ("Office Action"), the Examiner noted the lack of specific reference to the earlier application to which priority is claimed in the current application, rejected claims 24-25 under 35 U.S.C. § 112, second paragraph, rejected claims 21-23 and 30-31 under 35 U.S.C. § 102(b) as being anticipated by Weiler et al., Analytical Biochemistry, 1996, 243: 218-227 ("Weiler"), and rejected claims 21-36 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,184,347, claims 1-19 of U.S. Patent No. 6,300,137, and claims 4-24 of U.S. Patent No. 6,451,998.

Applicants' representative has amended the specification of the current application to specifically refer to the earlier application to which priority is claimed. With regard to the 35 U.S.C. § 112, second paragraph rejections, Applicants' representative finds the phrase "wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized" in the preamble of claim 24, prior to each reference to "each cell of the high-density array." Applicants' representative thus does not understand why the Examiner has identified a lack of antecedent basis for the phrase "each cell of the high-density array." The "each cell" is a cell of the high-density array, as clearly specified in the preamble of claim 24. Applicants' representative would be happy to amend the claims to correct an antecedent basis problem if the Examiner can kindly provide an explanation as to why the occurrence of the phrase "wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized" is not a sufficient basis for subsequent references to "each cell."

With regard to the 35 U.S.C. § 102(b) anticipation rejection, Applicants' representative confesses to be puzzled by the Examiner's citing of Weiler. In claim 21, Applicants claim the step of "applying the reactive wash solution to the surface of the solid substrate in order to react with, and deactivate, any unreacted reactive reagents," and in claim 30, Applicants claim the step of "applying a reactive wash solution to the surface of the solid substrate to react with, and deactivate, any remaining reactive monomers on the surface of the

solid substrate." In the cited sections of page 20, Weiler describes washing the rows of the polypropylene sheet with acetonitrile, in one case, and, in another case, with *successive* application of, first, dimethylformamide, then methanol, and finally with acetone. If the Examiner will please look at Figure 6 in U.S. Patent No. 6,184,347 ("Perbost I"), the Examiner will see that, with respect to the first case, acetonitrile is a wash agent well-known in the prior methods for solid-substrate oligonucleotide sysnthesis, and one clearly described example of a wash agent that does not react with, and deactivate any reacted reactive reagents. In the second case, the polypropylene sheet is first washed with DMF, presumably removing unreacted reagents and potentially causing the blooming that the invention claimed in Perbost I is directed to prevent. Only as a second, separate wash step is methanol used. The sequence of washing described in Weiler thus does not conform to the claim limitation that the solution applied to remove unreacted reagents is reactive towards, and deactivates the unreacted reagents preventing the reactive reagents from migrating to portions of the substrate to which they were not applied, and where they can undergo undesirable reactions. Please note that each of the modified wash steps, shown in Figures 10A-C of Perbost I, involve washing the substrate to remove unreacted reagents with the reactive wash solution in order to prevent migration of unreacted reagents which could then cause the blooming phenomenon. Once a wash step with an unreactive wash solution is undertaken, undersirable migration of unreacted reagents occurs, regardless of whether or not a reactive wash reageant is later applied.

The cited portions of page 222 and 223 of Weiler suggest using a different combination of capping reagents that do not include terahydrofuran, and teaches nothing about wash reagents. Note that capping reagents are applied in steps distinct from washing steps (for example, capping steps 606 and 622 in Figure 6 of Perbost I, distinct from washing steps 608 and 624). A wash step is employed to remove reactant solutions from the surface of a microarray, while a capping step introduces a solution containing reactants designed to covalently modify function groups of nascent oligonucleotides by bonding protecting moieties to the functional groups that can be subsequently removed in deprotecting steps. The current application is not concerned with, or directed to, capping reagents and capping steps. As clearly claimed in claims 21 and 30, the current application is directed to, and explicitly

claims, a reactive *wash* solution for removing a previously applied raction solution from the surface of a microarray.

Finally, please note that certain of the chemistries described in Weiler are different from those described in Perbost I. Applicants' representative believes that it would be improper to extend assumptions about the reactivities of reagents in one system to a different chemical system without a teaching in the second system that the reagents show similar reactivities in that system, or without a reference to a published paper or text that teaches that the reactivities in the second system are similar to those in the first system.

Thus, Applicants' representative cannot find a basis for an anticipation rejection of independent claims 21 and 30 based on Weiler. Applicants' representative therefore believes that independent claims 21 and 30, and dependent claims 22-23 and 31 that depend from them, are not anticipated by Weiler.

With regard to the obviousness-type double patenting rejection with respect to Perbost I, a separate terminal disclaimer in compliance with 37 CFR 1.321(c) is enclosed. With regard to the obviousness-type double patenting rejections with respect to Perbost, U.S. Patent No. 6,451,998 ("Perbost II") and Earhart et al., U.S. Patent No. 6,300,137 ("Earhart"), Applicants' representative admits to being respectfully puzzled. Earhart does not claim, in claims 1-19, use of a reactive wash reagent. Earhart is directed to using covering volumes during synthesis of probes on the surfaces of microarrays. While claim 3 of Earhart specifically claims various rinsing steps, the wash solution is not claimed. In the specification, the wash solution is explicitly mentioned as being acetonitrile (see, for example, line 29 of column 7). Perbost II is directed to, and claims, a modified capping reagent – a β- or γ-phosphoramidyl, protected alcohol. As discussed above, a capping reagent is not a reactive wash solution, and a capping step employed during oligonucleotide synthesis is not a wash step. The Examiner may consult Perbost I, Earhart, and many other resources that describe the steps of solid-state oligonucelotide synthesis via phosphoramidite chemistries to see that wash steps are clearly different from, and differentiated in the references from, capping steps and other such steps of the synthetic methods. Applicants are more than happy to file terminal disclaimers with respect to issued patents, such as Perbost I, that are fairly directed to, and that claim, a method related to the wash method claimed in the current application. However, Applicants are reluctant to file terminal disclaimers with

respect to completely unrelated issued patents. Applicants' representative therefore wishes to defer filing terminal disclaimers with respect to Perbost II and Earhart at this time, preferring to let the Examiner again review those issued patents in light of the above comments.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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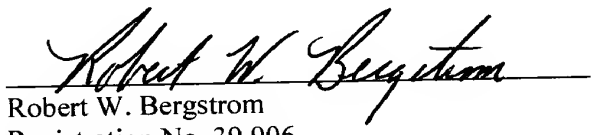
OLYMPIC PATENT WORKS PLLC



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Terminal Disclaimer
Extension of Time

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Version with Markings to Show Changes Made

In the Specification:

Page 1, line 5, the following new paragraph has been added:

Cross-Reference

This application is a continuation of Patent No. 6,184,347 issued February 6, 2001.